Reprogramming of Fibroblasts From Older Women With Pelvic Floor Disorders Alters Cellular Behavior Associated With Donor Age.

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Public Summary:
Our long term goal is to understand what causes urinary incontinence and pelvic organ prolapse in women and apply this information to design stem cell therapies for these conditions. Our primary goal in the current study was to test whether we could genetically reprogram cells from the vagina of women with urinary incontinence and prolapse into stem cells. We also examine whether the age of the female donor has any effect on the stems cells derived from genetic reprograming. These data are important in determining if we can use the patient as source of stem cells to treat her condition. We found that vaginal cells from affected women can be successfully reprogramed into stem cells, regardless of donor age. Further, cells that are differentiated from these stem cells did not show signs of aging when compared to the original cells from the donor. These data suggest that patients may be able to serve as their own donors for stem cell therapies, and that the cells derived from this type of process may possess “rejuvenated” functional characteristics. Hence, when implanted into the donor, these cells may improve function in addition to replacing lost cells or tissues.

Scientific Abstract:
We aimed to derive induced pluripotent stem cell (iPSC) lines from vaginal fibroblasts from older women with pelvic organ prolapse. We examined the effect of donor age on iPSCs and on the cells redifferentiated from these iPSCs. Vaginal fibroblasts were isolated from younger and older subjects for reprogramming. iPSCs were generated simultaneously using an excisable polycistronic lentiviral vector expressing Oct4, Klf4, Sox2, and cMyc. The pluripotent markers of iPSCs were confirmed by immunocytochemistry and quantitative reverse transcription-polymerase chain reaction (qRT-PCR). Spectral karyotyping was performed. The ability of the iPSCs to differentiate into three germ layers was confirmed by embryoid body and teratoma formation. Senescence marker (p21, p53, and Bax) expressions were determined by qRT-PCR and Western blot. The iPSCs were redifferentiated to fibroblasts and were evaluated with senescence-associated beta-galactosidase (SA) activity and mitotic index using time-lapse dark-field microscopy. iPSCs derived from both the younger and older subjects expressed pluripotency markers and showed normal karyotype and positive teratoma assays. There was no significant difference in expression of senescence and apoptosis markers (p21, p53, and Bax) in iPSCs derived from the younger subject compared with the older subject. Furthermore, fibroblasts redifferentiated from these iPSCs did not differ in SA activity or mitotic index. We report successful derivation of iPSCs from women with pelvic organ prolapse. Older age did not interfere with successful reprogramming. Donor age differences were not observed in these iPSCs using standard senescence markers, and donor age did not appear to affect cell mitotic activity in fibroblasts redifferentiated from iPSCs.